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DIALOG(R)File 155:MEDLINE(R)

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08168705 94141069

IgE epitopes on the **cat** (*Felis domesticus*) major allergen Fel d I:
a study with overlapping synthetic peptides.

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J Allergy Clin Immunol (UNITED STATES) Jan 1994, 93 (1 Pt 1) p34-43,
ISSN 0091-6749 Journal Code: H53

Languages: ENGLISH

Document type: JOURNAL ARTICLE

BACKGROUND: The major **cat** allergen Fel d I is composed of two
disulfide-linked polypeptide chains, chain 1 (70 amino acid residues) and
chain 2 (92 amino acid residues). Reduction and alkylation of Fel d I
eliminates almost all antigenic and allergenic activity, and detection of
linear epitopes with synthetic peptides is therefore not expected. METHODS:
We synthesized synthetic peptides of both chains of about 14 amino acid
residues, overlapping by 7 residues. The peptides were coupled to Sepharose
(Pharmacia, Uppsala, Sweden) and tested with sera of patients with
cat allergy. RESULTS: Three peptides showed specific binding of
human IgE, residues 25-38 and 46-59 of chain 1 and residue 15-28 of chain
2. IgE binding was inhibited by Fel d I and the corresponding **peptide**
. Of 61 patients with **cat allergy** tested, 65% showed IgE
binding to at least one of the peptides; 46% showed IgE binding to
peptide 25-38, 11% to **peptide** 46-59, and 28% to **peptide**

15-28. Each **peptide** was recognized by only one of the 78 patients
with negative RAST results. By affinity chromatography with **peptide**
-Sepharose anti-Fel d I antibodies were isolated, also confirming the
specificity of IgE binding to the peptides. The percentage of IgE
antibodies against Fel d I reactive with the peptides varied with the serum
and the **peptide** -Sepharose used and ranged from 2% to 55%.

CONCLUSIONS: Because the affinity of IgE binding to the peptides was very
low and only serum samples with high titers of Fel d I-specific IgE
antibodies (RAST 4+/5+) showed significant binding, these peptides are not
suitable for diagnostic purposes. However, the peptides are useful tools
for comparing IgE and IgG responses and for studying the relationship to

08999646 97276873

Integrated clinical experience with tolerogenic peptides.

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Int Arch Allergy Immunol (SWITZERLAND) May-Jul 1997, 113 (1-3) p326-8,
ISSN 1018-2438 Journal Code: BJ7

Languages: ENGLISH

Document type: JOURNAL ARTICLE

More than 2,000 patients have been dosed in the clinical development programs for Allervax **Cat** and Ragweed products in North America, Europe and Japan. Two peptides derived from Fel d 1 and three peptides derived from Amb a 1 were selected for clinical development following T cell epitope mapping of these major allergens. Clinical activity has been demonstrated in several dose regimens containing 75 and 750 microg of each component **peptide** given in 4-6 doses over 2-4 weeks. Greater activity has been seen with higher doses. Immediate hypersensitivity to treatment peptides is rarely seen and can be avoided through patient screening. A putative pathway resulting in histamine-mediated but IgE-independent allergic symptoms, similar in nature and severity to natural allergen exposure, has been identified in association with treatment. These manifestations are more pronounced in **cat** than ragweed **allergy** and are consistent with the respective diseases. When desired, the symptoms may be ameliorated with administration of H1 blockers prior to symptom appearance. The seasonal rise in allergen-specific IgE is blunted in association with therapy. Antigen-specific antibody levels (IgE and IgG), T cell primary proliferation and immediate skin test sensitivity will be followed in longer-term studies.

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08841858 97093614

Definition of the human T-cell epitopes of Fel d 1, the major allergen of the domestic **cat**.

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J Allergy Clin Immunol (UNITED STATES) Nov 1996, 98 (5 Pt 1) p884-94,
ISSN 0091-6749 Journal Code: H53

Languages: ENGLISH

Document type: JOURNAL ARTICLE

BACKGROUND: A heterodimeric acidic glycoprotein (Fel d 1) has been defined as the major allergen of the domestic **cat**. Because T-cell help is required for the initiation and maintenance of allergic responses, it is of importance to determine the T-cell-reactive regions of the Fel d 1 molecule. METHODS: Overlapping peptides corresponding to the two chains of Fel d 1 were tested in proliferation assays on polyclonal T-cell lines and for the ability to bind Fel d 1-specific IgE in ELISA and histamine release assays. RESULTS: Assay of T-cell lines derived from 53 subjects allergic to cats demonstrated that the majority of T-cell reactivity is found in chain 1 of Fel d 1. Two peptides (Fel-1 and Fel-2) containing major epitopes, alone or as a mixture, efficiently activated T cells and exhibited minimal detectable reactivity with IgE by ELISA or histamine release assay. CONCLUSIONS: Two Fel d 1 peptides containing major T-cell epitopes have been identified, have been shown to bind minimal Fel d 1-specific IgE, and are now being tested for the ability to decrease T-cell responses in patients with **cat allergy** as a new form of immunotherapy.

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08356492 95337754

Peptide-mediated immunoregulation.

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Medicine, London, UK.

Int Arch Allergy Immunol (SWITZERLAND) May-Jun 1995, 107 (1-3) p275-7,
ISSN 1018-2438 Journal Code: BJ7

Languages: ENGLISH

Document type: JOURNAL ARTICLE; **REVIEW**; REVIEW, TUTORIAL

Quantitative and qualitative characteristics of the signals received by a T cell determine whether receptor ligation results in cell activation, cell death, or the induction of antigen-specific non-responsiveness. Environmental factors such as the nature of costimulation, antigen-presenting cell type, peptide structure and cytokine levels also influence the differentiation of CD4+ helper T cells into functionally distinct subsets, which now appear pivotal in many immune-mediated disorders, including autoimmunity and **allergy**. Selective manipulation of the immune response, such as the functional inactivation or deviation of the cytokine secretion patterns of specific T cells, may be an effective

AU Morgenstern, Jay P.; Griffith, Irwin J.; Brauer, Andrew W.; Rogers, Bruce L.; Bond, Julian F.; Chapman, Martin D.; Kuo, Mei Chang
CS ImmuLogic Pharm. Corp., Cambridge, MA, 02139, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1991), 88(21), 9690-4
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB The complete primary structure of Fel dI (International Union of Immunol. Societies nomenclature), the major allergen produced by the domestic cat, *Felis domesticus*, was detd. by protein sequence anal. and cDNA cloning. Protein sequencing of Fel dI from an immunoaffinity-purified ext. of house dust revealed that the allergen is composed of 2 polypeptide chains. Degenerate oligonucleotides derived from the protein sequence were used in polymerase chain reaction amplification of cat salivary gland cDNA to demonstrate that the 2 chains are encoded by different genes. Chain 1 of Fel dI shares amino acid homol. with rabbit uteroglobin, while chain 2 is a glycoprotein with N-linked oligosaccharides.
IT **136796-93-5**, 23-92-Glycoprotein TRFP (Felis catus chain 1 isoform A protein moiety reduced) **136796-96-8**, Glycoprotein TRFP (Felis catus chain 1 isoform A protein moiety reduced) **136796-97-9**, Glycoprotein TRFP (Felis catus chain 1 isoform B protein moiety reduced)
(amino acid sequence of)
L3 ANSWER 5 OF 5 HCA COPYRIGHT 1995 ACS
AN 115:205920 HCA
TI A human T-cell-reactive feline protein (trfp) isolated from house dust and uses therefor
IN Gefter, Malcolm L.; Garman, Richard D.; Greenstein, Julia L.; Kuo, Mei Chang; Rogers, Bruce L.; Brauer, Andrew W.
PA ImmuLogic Pharmaceutical Corp., USA
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
PI WO 9106571 A1 910516
DS W: AU, CA, DK, FI, JP, NO
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE
AI WO 90-US6548 901102
PRAI US 89-431565 891103
DT Patent
LA English
AB TRFP, a glycoprotein isolated and affinity purified from house dust of homes with cats, is useful in diagnosis and therapy of cat allergies. It has 2 covalently-linked chains and a mol. wt. of .apprx.40,000. The protein and cDNA sequences were detd. Chain 1 has 2 alternative leader sequences, which, in the genomic DNA, are closely linked at the 5' end of the structural gene. There was tissue-specific expression of 2 different mRNA forms for chain 2 in cat skin and salivary gland (chain 2 short and chain 2 long, resp.); the cat genome had different gene segments encoding both forms. TRFP has sequence microheterogeneity as well. Recombinant TRFP was

expressed in Escherichia coli. Most of the TRFP protein contains T-cell epitopes capable of stimulating T-cells in individuals with cat allergies, however, there are major differences in the strength of the elicited T-cell response obtained with different portions of the TRFP mol. Each epitope worked in some individuals and each individual had a characteristic response pattern. The most dominant T-cell epitopes were contained in the Fel 8 peptide (residues 1-30 of chain 1). TRFP and peptides induced anergy in antigen-specific T-cell lines.

- IT 136796-93-5, 23-92-Glycoprotein TRFP (Felis catus chain 1 isoform A protein moiety reduced)
(amino acid sequence of, diagnosis and treatment of cat allergy in relation to)
- IT 136796-96-8 136796-97-9
(human T cell-reactive feline protein sequence contg., for diagnosis and treatment of cat allergy)
- IT 136380-55-7 136380-56-8 136380-69-3
136380-72-8 136380-73-9 136414-74-9
(peptide of chain 1 of human T-cell reactive feline protein, cat allergy human T-cell response to)